REMARKS

Claims 1 and 3-6 remain in the application.

Claim 1 has been amended to recite the administration of N-acetyl-L-glutamine *as a sole source* of glutamine from a liquid composition, support for which can be found, for example, in Applicant's specification at page 8, last paragraph.

Claim 1 has also been amended to recite the administration of N-acetyl-L-glutamine from a *nutritional* liquid, support for which can be found, for example, at p. 10, third paragraph.

Claim 5 has been amended to delete aluminum salts from the Markush listing of nutritionally acceptable salts of N-acetyl-L-glutamine.

Invention Synopsis

The method of the present invention is based upon the discovery that N-acetyl-L-glutamine has utility as an oral glutamine supplement in humans. It has now been found that human intestinal tissue deacetylates N-acetyl-L-glutamine, to thus form glutamine for use in the body. As such, N-acetyl-L-glutamine can now be incorporated into oral nutritionals designed for human consumption to thus provide a source of supplemental glutamine. This is especially useful in liquid formulations where N-acetyl-L-glutamine is more stable than free glutamine. Free glutamine is more commonly used in solid or powder product forms.

Applicant found that orally administered N-acetyl-L-glutamine is a highly effective glutamine source, more so than even glutamine itself when administered orally. Applicants conducted a study to evaluate, among other effects, the potential impact of orally administered N-acetyl-L-glutamine versus glutamine on intestinal damage caused by protein-energy malnutrition in pigs. It was found that the deleterious effects of malnutrition on the antioxidant defense system appeared less marked in the intestine of animals that orally consumed the N-acetyl-L-glutamine supplement than in the animals that orally consumed caseinate or glutamine supplements (see Applicant's Specification at page 40, second paragraph.). It was also found that oral N-acetyl-L-glutamine was significantly more effective than caseinate as well as glutamine (oral) in reducing small intestine immunological changes promoted by malnutrition, especially in total cell number and B and T helper subpopulations (see Applicants' Specification at page 41, fourth paragraph).

The data from the study therefore suggest orally administered N-acetyl-L-glutamine would be a surprisingly effective source of nutritional glutamine, more so than even free glutamine itself when administered orally.

Double Patenting Rejection

Claims 1 and 3-6 have been rejected under the judicially created doctrine of obviousness-type double patenting as unpatentable over claims 1-6 of copending Application No. 10/266,317. Applicants traverse this rejection. Claims 1-6 of the cited copending application, however, have since been withdrawn as non-elected claims pursuant to a restriction requirement. Withdrawal of this rejection is requested.

Rejection under 35 USC 103(a)

Claims 1 and 3-6 have been rejected under 35 USC 103(a) as being unpatentable over Ziegler et al. in view of either one of JP 58-018320 ('320) or JP 55-105652 ('652). Applicant traverses this rejection as it would apply to the amended claims.

Ziegler et al. disclose parenteral nutrition comprising L-glutamine to improve nitrogen retention and reduce hospital morbidity after bone marrow transplant.

The '320 reference discloses N2-acetyl-L-glutamine-aluminum complex as an antiulcer agent. The complex is combined with small organic acids to improve stability and eliminate the astringent taste of the aluminum complex.

The '652 reference discloses a method of purifying N-acetyl-L-glutamine for use as an antiulcer drug.

None of the prior art references teach the use of N-acetyl-L-glutamine as a nutritional source of glutamine. The JP references disclose aluminum salts or complexes of N-acetyl-L-glutamine for use as antiulcer drugs, while Ziegler et al. disclose only the administration of L-glutamine itself.

Of course, since none of the references disclose the use of N-acetyl-L-glutamine as a nutritional source of glutamine, none of the references teach the use of N-acetyl-L-glutamine from a nutritional composition. The methods of the present invention are limited to the use of N-acetyl-L-glutamine from an oral *nutritional composition.*

The JP references are also specific to aluminum salts and complexes, which are well known for treating or preventing of gastric ulcers. These two references are silent, however, as to other salt forms. The method of the present invention, by contrast, has been amended to exclude aluminum salts from the recited Markush, to further distinguish from the JP references.

None of the references specifically teach oral administration, which is a key limitation of the method claims of the present invention. Ziegler et al. teaches parenteral administration. The JP references are completely silent as to administration routes.

Applicants submit that the prior art references fail to teach, suggest or motivate the skilled artisan to combine the various limitations of the present claims. In particular, there is no suggestion within any of the references that N-acetyl-L-glutamine could be used as a substitute for glutamine itself, for any purpose. There is certainly no suggestion from any reference to combine N-acetyl-L-glutamine in an oral nutritional formula such as that recited in the present method claims.

Applicants also submit that the claimed method produces unexpected results. As noted above, it was found that orally administered N-acetyl-L-glutamine is a highly effective glutamine source, more so than even glutamine itself when administered orally. Applicants conducted a study to evaluate, among other effects, the potential impact of orally administered N-acetyl-L-glutamine versus glutamine on intestinal damage caused by protein-energy malnutrition in pigs. It was found that the deleterious effects of malnutrition on the antioxidant defense system appeared less marked in the intestine of animals that orally consumed the N-acetyl-L-glutamine supplement than in the animals that orally consumed caseinate or glutamine supplements (see Applicant's Specification at page 40, second paragraph). It was also found that oral N-acetyl-L-glutamine was significantly more effective than either caseinate or glutamine (oral) in reducing small intestine immunological changes promoted by malnutrition, especially in total cell number and B and T helper subpopulations (see Applicants' Specification at page 41, fourth paragraph).

In short, none of the prior art references teach that orally administered N-acetyl-L-glutamine would be effective as a glutamine supplement, and certainly none suggest the findings of the

above-data, that orally administered N-acetyl-L-glutamine is a more effective source of nutritional glutamine than orally administered glutamine itself.

In view of the amendments presented and the foregoing remarks, Applicant respectfully requests withdrawal of this rejection as it would apply to the remaining amended claims.

Conclusion

Applicant respectfully requests reconsideration of this application and allowance of claims 1 and 3-6.

Respectfully submitted,

by William J. Winter
Attorney for Applicant
Registration No. 36,060

Abbott Laboratories,
Ross Products Division
Department 108140/S1
625 Cleveland Avenue
Columbus, OHIO 43215-1724
Phone (614) 624-5686;
Fax (614) 624-3074